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## Original Research Article

# The relationship between eosinophil and nondipper hypertension



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## ABSTRACT

**Aims:** Non-dipper hypertension is associated with increased cardiovascular morbidity and mortality. It is known that eosinophils play an important role in vasoconstriction and thrombosis. We aimed to compare the numbers of eosinophil counts of the patients nondipper versus dipper hypertension.

**Materials and method:** This study included 70 hypertensive patients. Hypertensive patients were divided into two groups: 35 dipper patients (15 male, mean age  $50.94 \pm 11.13$  years) and 35 non-dipper patients (10 male, mean age  $56.11 \pm 11.05$  years). Concurrent routine biochemical tests and eosinophil count on whole blood count were performed on these patients. These parameters were compared between groups.

**Results:** No statistically significant difference was found between two groups in terms of basic characteristics. Baseline characteristics of the study groups were comparable. Nondipper patients had a higher eosinophil and MPV value than dipper patients ( $148.86 \pm 80$  vs.  $304.57 \pm 182$  and  $7.8 \pm 0.12$  vs.  $9.2 \pm 0.2$  fl  $p < 0.001$ , respectively).

**Conclusion:** Eosinophil count and MPV value are higher in patients with nondipper hypertension when compared to the dippers.

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## 1. Introduction

Non-dipper hypertension is associated with increased cardiovascular morbidity and mortality, including stroke, myocardial infarction, and sudden cardiac death [1,2]. It is known that eosinophils play an important role in endothelial dysfunction, vasoconstriction, inflammation and thrombosis [3,4]. Eosinophils stimulate the activation and aggregation of platelets. Moreover, they ease the formation of thrombosis via inhibition of thrombomodulin [5–7].

Systolic and diastolic blood pressures decrease more than 10% during sleep compared to daytime. This diurnal pattern

is considered to be normal. The term ‘nondipper’ refers to patients whose blood pressure does not demonstrate this diurnal pattern. Nondipper patients have a higher cardiovascular risk and target organ damage than dippers [8,9].

The powerful vasoconstrictor and procoagulant effects of eosinophils made us hypothesize that there might be a correlation between eosinophil concentration and nondipper hypertension. Dipper and nondipper blood pressure patterns have been studied extensively among hypertensive patients. As far as we know, there is no study performed until today about the association of blood eosinophil concentration with dipper and nondipper hypertension. In our study, we compared

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**Table 1 – Comparison of basic clinical and demographic characteristics and ambulatory blood pressure monitoring features of dipper and nondipper hypertensive patients.**

	Dipper (n=35)	Nondipper (n=35)	p Value
Age (years)	50.94 ± 11.13	56.11 ± 11.05	0.06
Sex (n, %) males	15	10	0.62
BMI (kg/m <sup>2</sup> )	28.9 ± 3.4	29.4 ± 3.49	0.59
Smoking	10 (20%)	7 (20%)	0.25
Heart rate (beats/min)	72 ± 11.5	78 ± 19	0.32
Mean SBP (mm Hg) (awake)	137.4 ± 14	139.6 ± 35.4	0.73
Mean DBP (mm Hg) (awake)	84.73 ± 10.34	84.95 ± 12.33	0.98
Mean SBP (mm Hg) (sleep)	115.1 ± 19.2	140.4 ± 18.1	<0.001
Mean DBP (mm Hg) (sleep)	68.6 ± 9.5	80.9 ± 10	<0.001

BMI: body mass index, SBP: systolic blood pressure; DBP: diastolic blood pressure.

eosinophil counts, between dipper and nondipper hypertensive patients.

## 2. Materials and method

### 2.1. Selection of the patients

One hundred patients were screened and 30 patients were excluded from the study for various reasons. The remaining 70 patients with a history of chronic hypertension and receiving appropriate antihypertensive medications for at least 3 months prior to enrollment were prospectively enrolled. The blood pressure was measured in the nondominant upper limb of the patient while the patient was seated, after a 5-min rest. The blood pressure of the patients was measured. The patients having a systolic blood pressure  $\geq 140$  mm Hg and/or a diastolic blood pressure  $\geq 90$  mm Hg and those taking antihypertensive drugs were accepted to be hypertensive.

Physical examination, medical history of patients, and blood biochemistry were evaluated in all groups to exclude systemic diseases. Patients with coronary artery disease, chronic renal failure, chronic liver disorders, chronic lung disease, moderate or severe valvular disease, diabetes mellitus, congenital heart disease, left ventricular systolic dysfunction on echocardiography (EF < 50%), recent acute coronary syndrome, anemia, pregnancy, obstructive sleep apnea, secondary hypertension, hematological disorders, known malignancy, thyroid dysfunction, hypercholesterolemia, electrolyte imbalance, and drug history included anti-gout agent, antiinflammatory agent (steroid or nonsteroid), antiaggregant or anticoagulant agents and antihistaminic agents were excluded from the study. Also patients having a recent history of an acute infection or high body temperature  $> 38$  °C, an inflammatory or allergic disease were excluded from the study.

### 2.2. Ambulatory 24-h blood pressure monitoring

Ambulatory 24-h blood pressure monitoring was performed. Automatic blood pressure recordings were obtained regularly every 30 min during the 24-h period. The cuff was placed around the nondominant arm of the subjects. Sleep and awake periods were assessed based on the information obtained from the patients. Nocturnal blood pressure dipping was calculated

using the following formula:  $[\%] \ 100 \times [1 - \text{[sleep systolic blood pressure/awake systolic blood pressure]}]$ . Nocturnal blood pressure dipping was defined as more than 10% decrease in both nocturnal systolic and diastolic blood pressures compared to the average daytime blood pressures. Detection of less than 10% decrease in either systolic or diastolic blood pressures was regarded as nondipper hypertension.

### 2.3. Laboratory tests

Biochemical parameters were analyzed spectrophotometrically on ArchitectC16000 [Abbott, USA] autoanalyzer using enzymatic-colorimetric assay.

For whole blood count [eosinophil count, Hematocrit, Hemoglobin, MCV, MPV, leukocytes, platelets], the blood samples were collected in tubes with EDTA and these blood samples were analyzed in 2 h after vein puncture. Hematological parameters, including hemoglobin (Hb), WBC count, and platelet count, were also analyzed on CELL-DYN 3700 [Abbott, USA] device using impedance and optic scatter method.

### 2.4. Statistical analysis

SPSS 16.0 statistical program [SPSS Inc., Chicago, IL, USA] was used for statistical study. All values are given as mean  $\pm$  standard deviation. Mean values of continuous variables were compared between groups using the Student's t test or Mann-Whitney U test, according to whether they were normally distributed or not, as tested by the Kolmogorov-Smirnov test. The chi-square test was used to assess differences between categorical variables. A p value less than 0.05 was considered significant.

## 3. Results

According to the 24-h ambulatory blood pressure monitoring, dipper and nondipper hypertension were found in 35 patients in both groups. Evaluating basic clinical and demographic characteristics, there was no statistically significant difference between two groups in terms of heart rate, age, gender distribution, body mass index and smoking status. In the dipper patients sleeping mean systolic and diastolic blood pressure were lower than nondipper patients ( $115.1 \pm$

**Table 2 – Comparison of biochemical and echocardiographical features of dipper and nondipper hypertensive patients.**

	Dipper (n=50)	Nondipper (n=35)	p Value
Fasting glucose (mg/dl)	93.5 ± 11	90.5 ± 9.8	0.52
Creatinine (mg/dl)	0.92 ± 0.12	1.1 ± 0.18	0.24
AST (U/L)	24.2 ± 4.5	23.7 ± 3.6	0.77
ALT (U/L)	23.9 ± 1.7	21.3 ± 2.4	0.65
Total cholesterol (mg/dl)	218.4 ± 45.1	209.6 ± 32.1	0.93
Na (mmol/L)	143 ± 15.6	139 ± 12	0.56
K (mmol/L)	4.3 ± 0.4	4.4 ± 0.3	0.66
TSH (μIU/mL)	1.65 ± 0.3	1.44 ± 0.3	0.65
LV ejection fraction (%)	62 ± 3.6	60.7 ± 6.7	0.27
LV enddiastolic diameter (mm)	46.1 ± 3	46.7 ± 3.6	0.11
LV endsistolic diameter (mm)	30.3 ± 3.5	31.3 ± 3.5	0.29
Left atrium diameter (mm)	33.5 ± 4.2	39.4 ± 8.6	0.06
LV mass index (g/m <sub>2</sub> )	111.6 ± 18.3	126 ± 28.2	0.001

AST: aspartate aminotransferase, ALT: alanine aminotransferase, TSH: thyroid-stimulating hormone, LV: left ventricular.

**Table 3 – Comparison of whole blood count features of dipper and nondipper hypertensive patients.**

	Dipper (n=50)	Nondipper (n=35)	p Value
Leukocyte (10 <sup>3</sup> /μl)	8732 ± 455	9223 ± 546	0.055
Eosinophil count (10 <sup>3</sup> /μl)	148.86 ± 80	304.57 ± 182	<0.001
Mean platelet volume (MPV) (fl)	7.8 ± 0.12	9.2 ± 0.20	<0.001
Mean corpuscular volume (MCV) (fl)	89.4 ± 2.1	88.8 ± 1.8	0.56
Hemoglobin (g/dl)	14 ± 1.5	13.4 ± 1.7	0.77
Hematocrit (%)	39.8 ± 3.8	39.7 ± 4.6	0.65
Platelet (10 <sup>3</sup> /μl)	263 ± 81	254 ± 57	0.1

19.2 vs. 140.4 ± 18.1 mm Hg, and 68.6 ± 9.5 vs. 80.9 ± 10 mm Hg;  $p < 0.001$ , respectively) (Table 1).

Left ventricular end-diastolic dimension, end-systolic dimension, left atrium dimension, and left ventricular ejection fraction were similar between the two groups ( $p > 0.05$ ). At left ventricular mass index was significantly higher in nondipper patients ( $p = 0.001$ ) (Table 2).

Given blood count parameters, in the group of nondipper patients blood eosinophil count, and MPV value, which were tested simultaneously in blood samples were significantly higher in comparison with the dipper group [ $p < 0.001$ ]. There was no statistically significant difference between two groups with regard to leukocyte count, platelet count, MCV, hemoglobin and hematocrit level (Table 3).

#### 4. Discussion

The present study showed that blood eosinophil count and MPV value are higher in patients with nondipper hypertension when compared to the dippers.

Increased cardiovascular morbidity and mortality have been demonstrated in patients with nondipper patients when compared to the dipper patients in previous studies [1,2].

In the nondipper hypertension, left ventricular diastolic function abnormalities, evidence of conduction disturbances, cardiac autonomic dysfunction, left ventricular hypertrophy and increase in the frequency of ventricular arrhythmia

have been described in these patients. Moreover, increased inflammatory activity, is proposed to be associated with the etiology and pathogenesis of cardiovascular diseases and arrhythmia in these patients [9–11].

Eosinophils cause coagulation system activation and platelet activation, also cause vasospasm such as coronary artery spasm. Umemeto et al. reported that peripheral eosinophil counts were significantly higher in patients with severe coronary spasm than nonspasm patients. Also speculated that eosinophil count could predict vasospastic angina pectoris [11]. Erdoğan et al. reported a significant higher eosinophil count in patients with angina pectoris than controls groups [12]. Additionally eosinophils play role in myocarditis and heart failure [13].

In our study we found significant differences in MPV between nondipper hypertensive patients and dipper group. Also, our findings are consistent with those of Inanç et al. [14]. Also we have found significant differences in eosinophil count between two groups.

As far as we know, there is no study available in the literature about the association between nondipper hypertension and eosinophil count.

When 2 groups were compared in our study, eosinophil count of the patients having nondipper hypertension was significantly higher than dipper hypertension groups.

Eosinophils are equipped with several granule-associated molecules which play a role in the occurrence of thrombosis and vascular injury. Eosinophils generate an increased

tendency to thrombosis through leukocyte, platelet stimulation and release of tissue factor [15–18]. All these effects contribute to procoagulation through preventing the activation of thrombin and endorsing fibrin formation. Eosinophils store and release tissue factor as well as other cationic proteins. Major basic protein, eosinophilic cationic protein, activates platelets and promotes thrombus formation by inhibiting thrombomodulin in hypereosinophilic syndromes and allergic diseases. In addition, antineutrophil cytoplasmic antibodies may shift the endothelial lining to proadhesive and prothrombotic surface [19,20]. Sakai et al. demonstrated that large thrombus has greater eosinophil counts both in thrombi and peripheral blood. Also speculated that thrombus growth might be facilitated in patients with higher eosinophil counts in peripheral blood [21].

Eosinophils play pulmonary and systemic vasoconstriction via the peroxidase–hydrogen peroxide/halide system. Activated eosinophils and secreted eosinophil granule proteins were most evident within the necrotic and later stage thrombotic lesions and were found mainly within the areas of acute tissue damage in the endocardium and in the walls of small blood vessels. These findings suggest that eosinophil granule proteins are involved in vascular injury, also eosinophils may affect cardiovascular system through inflammatory cell infiltration [11,22].

Recent studies showed that eosinophils were associated with stent thrombosis, stent restenosis and acute coronary syndromes. Furthermore, it was reported that elevated serum eosinophil concentration might be responsible for cardiac mural thrombus and embolic events [23–25]. Also Keceoğlu et al. speculated that higher eosinophil count is related to left atrial thrombus in patients with atrial fibrillation [26].

The powerful vasoconstrictor and procoagulant effects of eosinophils made us hypothesize that there might be a correlation between eosinophil concentration and nondipper hypertension. In the literature, there is no study investigating the association between nondipper hypertension and eosinophils. Our study is of importance with regard to this matter; we investigated the effect of eosinophil concentration on nondipper pattern among hypertensive patients.

The most important restriction of our study is the limited number of patients. Further studies are required to determine the relation between eosinophil count and nondipper hypertension.

In conclusion, the measurement of eosinophil count may be used to indicate the presence of nondipper pattern and increased risk of hypertension-related adverse cardiovascular events. Our results may contribute to etiopathogenesis of nondipper hypertension and pathophysiological mechanisms of increased prevalence of cardiovascular morbidity and mortality risk in these patients. Increased concentration of eosinophil might be explained with vasoconstriction and high blood pressure in nondipper patients.

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